



# Gastroesophageal reflux disease

16<sup>ème</sup> journée d'automne  
d'actualités en gastro-  
entérologie et hépatologie

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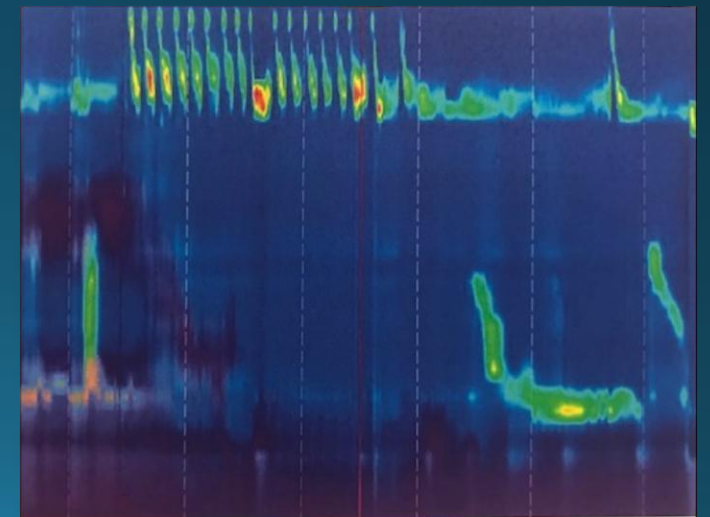
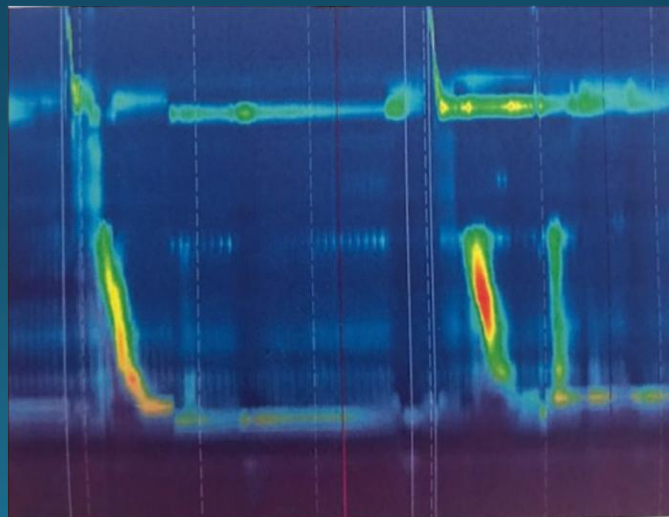
# Mrs M. J., 45 years old

- Epigastralgia, regurgitation and vomiting refractory to PPIs. Night cough preventing the use of CPAP.
- Medical history : Steinert myotonic dystrophy, right fronto-parietal stroke, sacral nerve stimulation implantation for fecal incontinence, hypercholesterolemia, obstructive sleep apnea syndrome.
- No alcohol or tobacco consumption.



# Mrs M. J., 45 years old

- OGD : sliding hiatal hernia (3 cm).  
Helicobacter pylori-negative.
- Scintigraphy exam. No significant delayed of gastric emptying.  
Gastric retention 30%, T=3h.
- Esophageal manometry. No esophageal contractions with incomplete bolus clearance to solids and hypotonia of upper esophageal sphincter (Chicago classification).



# Mrs M. J., 45 years old

- Impedance pH-metry  
Acid exposure **14.8** (N <4.2%). Total number of reflux episodes **198** (N <73). Score DeMeester **46.2** (N <14.7).
- Dexilant® 30 mg/d → to 60 mg/d. Motilium® 10 mg 3x/d.
- Persistent heartburn and trouble to perform CPAP
- OGD under double dose PPIs : reflux oesophagitis LA grade A.

# Which attitude do you propose?

- A) Double dose Dexilant® 60 mg  
2x/d + repeat OGD in 6-12 months
- B) EndoStim Electric Stimulator
- C) Anti-reflux surgery

# Attitude/clinical evolution

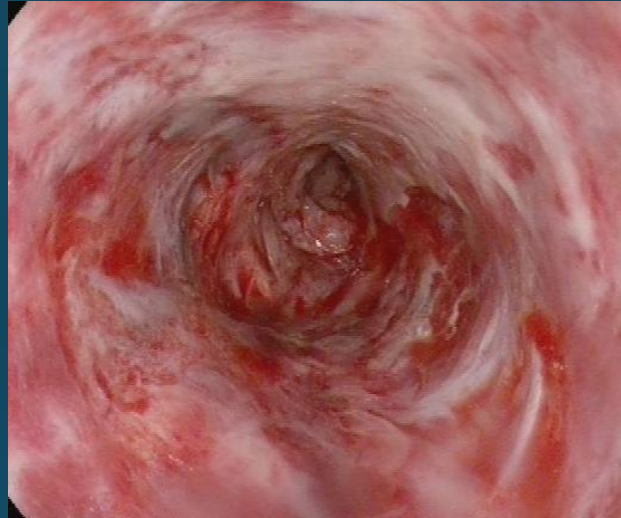
- LES Stimulation System, EndoStim, in view of esophageal motility disorder.
- Favorable evolution, resolution of symptoms (2 months later).

# Mrs N.-V. J., 58 years old

- Squamous cell right basi-lingual carcinoma, cT<sub>1</sub>N<sub>3</sub>M<sub>0</sub> stage IVB treated with chemotherapy (cisplatin/tirapazamine), radiotherapy and lymph node ablation in 2004.
- Hospitalized for acute confusional state with severe electrolyte disorders (Na 108 mmol/L, K 2.3 mmol/L, Ph 0.39 mmol/L) and protein-caloric malnutrition (BMI 16.2 kg/m<sup>2</sup>).
- Chronic dysphagia, retrosternal pain, abdominal pain, vomiting.
- Chronic alcoholism, active smoking (40 UPA).

# Mrs N.-V. J., 58 years old

- CT scan : oeso-gastric distension. No relapse of cancerous disease
- OGD :
- Reflux oesophagitis LA grade D.
- Suspicion of Barrett's esophagus (C16M16, Prague classification).
- Esophageal stricture (35-38 cm from dental arch) not crossable.
- Crossing of stricture after balloon dilatation up to 11 mm.
- Ulcerated lesion of the pylorus. Stricture of the bulb with an ulcer Forrest III.





# Mrs N.-V. J., 58 years old

- Repetitive dilatations of the esophagus stricture up to 18 mm (6 sessions).
- Histological analysis : intestinal metaplasia without dysplasia at the Z-line. No eosinophilic oesophagitis. No malignancy of pylorus and bulb.
- Initial EUS: signs of severe and stricturing panesophagitis without sign of cancer relapse or suspicious local lymph nodes.
- Nexium<sup>®</sup> 40mg 2x/d combined with Motilium<sup>®</sup> 10 mg 3x/d.

# Mrs N.-V. J., 58 ans

- Relapse of a significant stricture 2 weeks after the end of the sessions of balloon dilation.
- Placement of a Fully covered self-expanding metallic stent (SEMS), 10 cm in length.
- Spontaneous migration of the SEMS (2 weeks later).
- Endoscopic removal of the SEMS with a good calibration of the stricture.



# Evolution

- OGD+EUS (2 months later):
- Adequate calibration of stricture. Persistent reflux oesophagitis grade D with a stenosing bulb inflammation.
- Cystic dystrophy of the duodenal wall associated with chronic pancreatitis.
- Resolution of symptoms.
- Stop alcohol and smoking.
- Endoscopic placement of pancreatic prosthesis and calibration of pancreatic duct wirsung and HBD will be scheduled.

# Diagnostic workup

- Endoscopic presentation: 70% NERD, 30% ERD
- A presumptive diagnosis of GERD can be established in the setting of typical symptom of heartburn and regurgitation. PPI therapy is recommend in this setting
- A cardiac cause should be excluded in patients with chest pain before gastrointestinal evaluation
- No interest of barium radiographs
- Routine biopsies are not recommended to diagnose GERD
- Screening for *Helicobacter pylori* is not recommended



# Diagnostic workup

Diagnostic test	Indication	Highest level of evidence	Recommendation
PPI trial	Classic symptoms, no warning signs,	Meta-analysis	Negative trial does not rule out GERD
Barium swallow	Not for GERD diagnosis. Use for evaluation of dysphagia	Case-control	Do not use unless evaluating for complication (stricture, ring)
Endoscopy	Alarm symptoms, screening of high-risk patients, chest pain	Randomized Controlled Trial	Consider early for elderly, those at risk for Barrett's, non-cardiac chest pain, patients unresponsive to PPI
Esophageal biopsy	Exclude non-GERD causes for symptoms	Case-Control	Not indicated for diagnosis of GERD
Esophageal manometry	Preoperative evaluation for surgery	Observational	Not recommended for GERD diagnosis. Rule out achalasia/scleroderma-like esophagus prep
Ambulatory reflux monitoring	Preoperatively for non-erosive disease. refractory GERD symptoms, GERD diagnosis in question	Observational	Correlate symptoms with reflux, document abnormal acid exposure or reflux frequency

GERD, gastroesophageal reflux disease; PPI, proton pump inhibitor.



## Indication for endoscopy

Dysphagia

Weight loss

Refractory symptoms

Evaluations for Barrett's

- Age > 50
- Years of GERD
- White, male
- Obese

# Novelties in impedance PH metry

New impedance parameters for GERD diagnosis in patients with endoscopy-negative heartburn.

- Postreflux Swallow-induced Peristaltic Wave (PSPW) index
- Mean Nocturnal Baseline Impedance (MNBI)

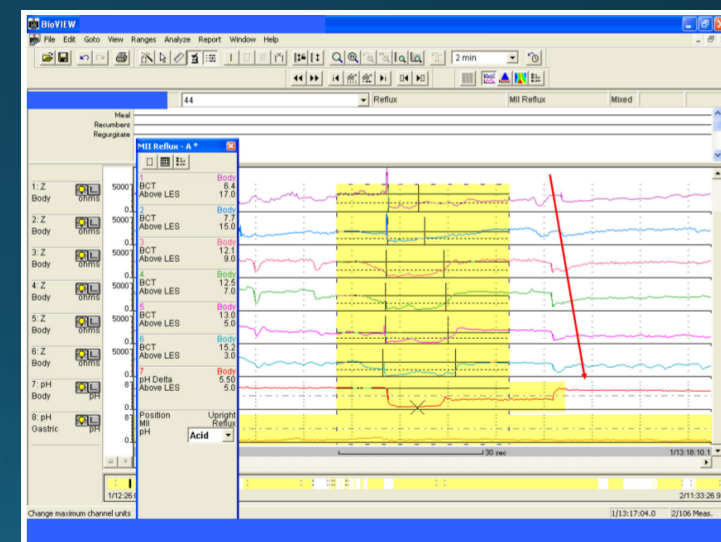
**Table 2** Assessment, calculation, and normal values of PSPW index and MNBI at impedance-pH monitoring

Assessment	Calculation	Normal values
<b>PSPW index</b> Reflex events followed by a PSPW within 30 s are summed by means of a digital counter, while the number of total refluxes is automatically provided by the software at the end of the manual review	Number of total refluxes followed by a PSPW within 30 s divided by the number of total refluxes	>61% <sup>a</sup>
<b>MNBI</b> Selection of three 10-min nighttime recumbent periods with avoidance of reflux events, pH drops and swallows	Baseline impedance values in the three periods are summed, and the mean is calculated	>2292 Ohms <sup>a</sup>

## Advantages

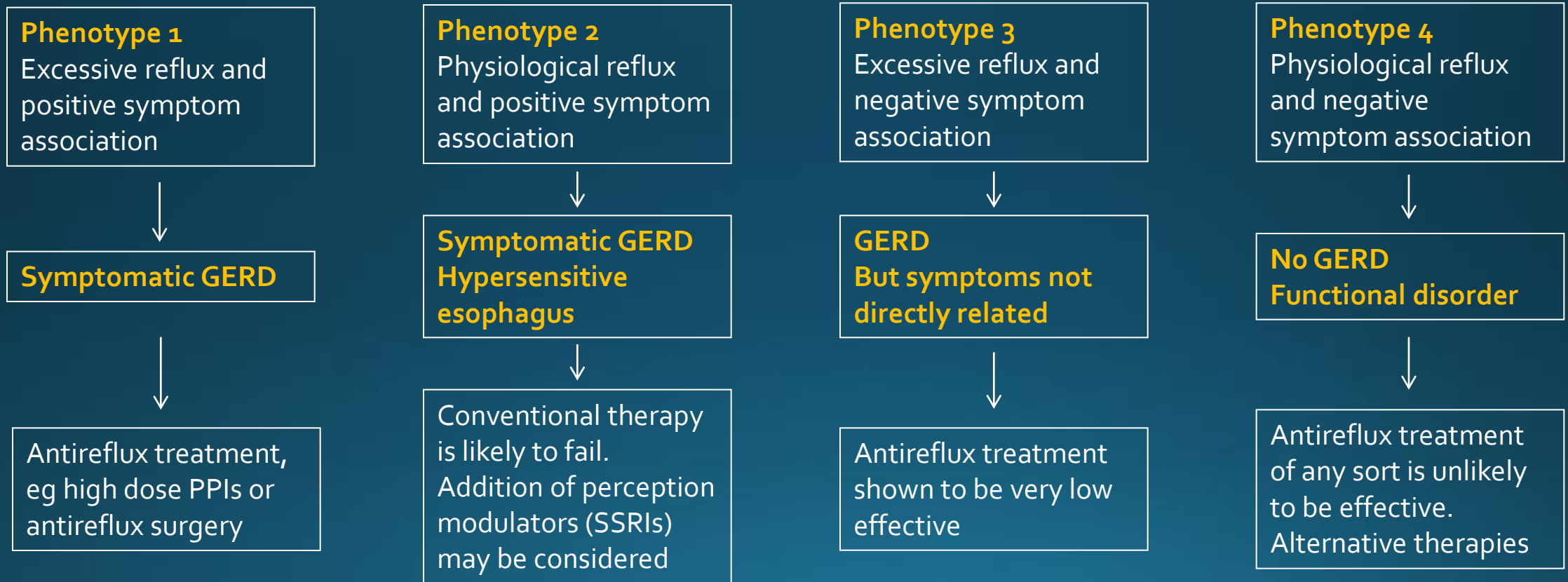
- Highly accurate in distinguishing reflux-related from reflux-unrelated heartburn
- Off- as well as on-PPI therapy

PSPW



# Impedance PH metry identifies 4 GERD phenotypes

## IPH monitoring after withholding PPI therapy



# Efficacy of lifestyle interventions

Lifestyle intervention	Effect of intervention on GERD parameters	Sources of data	Recommendation
Weight loss (46,47,48)	Improvement of GERD symptoms and esophageal pH	Case-Control	Strong recommendation for patients with BMI>25 or patients with recent weight gain
Head of bed elevation (50-52)	Improved esophageal pH and symptoms	Randomized Controlled Trial	Head of bed elevation with foam wedge or blocks in patients with nocturnal GERD
Avoidance of late evening meals (180, 181)	Improved nocturnal gastric acidity but not symptoms	Case-Control	Avoid eating meals with high fat content within 2-3 h of reclining
Tobacco and alcohol cessation (182-184)	No change in symptoms or esophageal pH	Case-Control	Not recommended to improve GERD symptoms
Cessation of chocolate, caffeine, spicy foods, citrus, carbonated beverages	No studies performed	No evidence	Not routinely recommended for GERD patients. Selective elimination could be considered if patients note correlation with GERD symptoms and improvement with elimination

BMI, body mass index; GERD, gastroesophageal reflux disease.



Proved improvement

Weight loss

Head of bed elevation

Avoidance of late evening meals

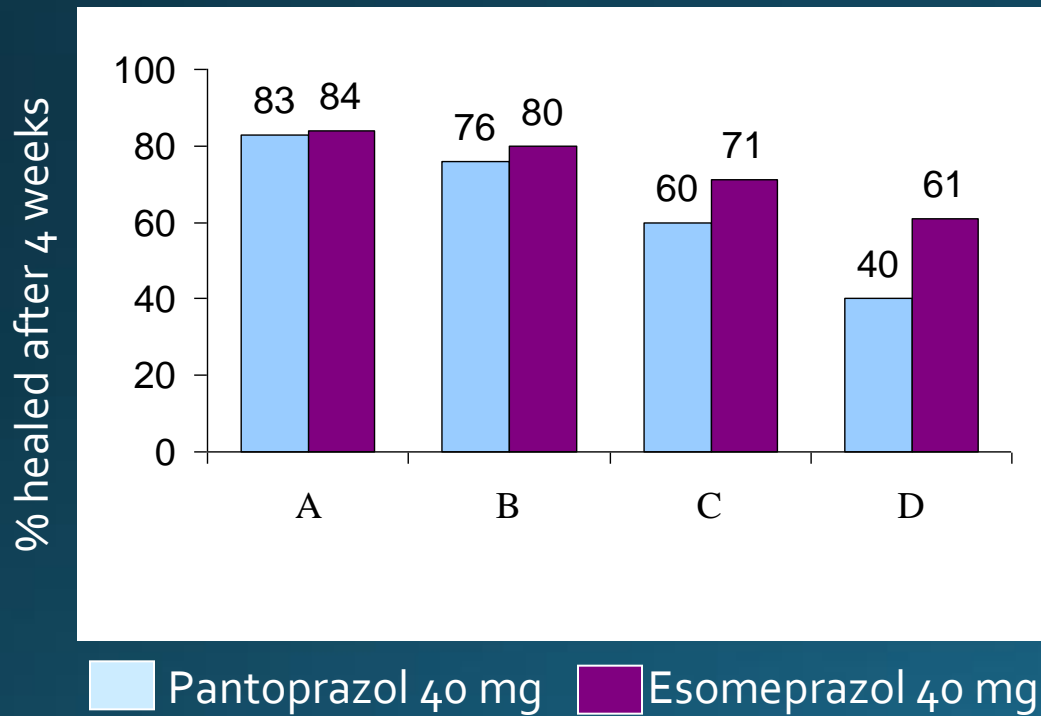


# Therapy

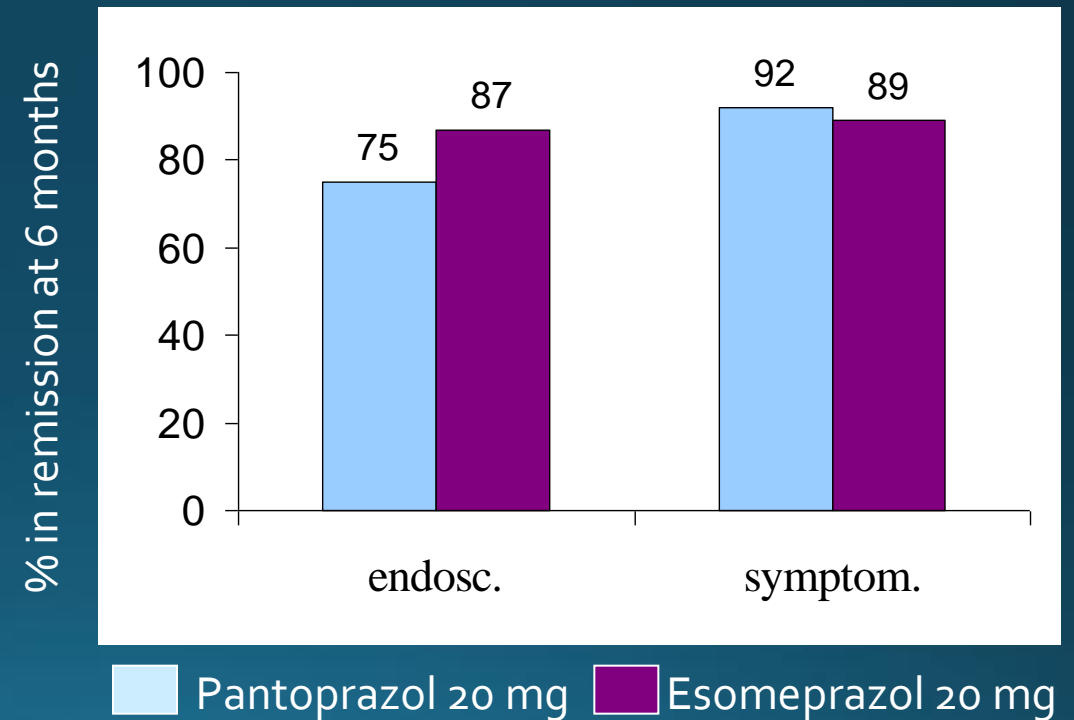
- PPI therapy is effective in typical GERD
- An 8 week course of PPI is the therapy of choice for symptom relief and healing of ERD and NERD with abnormal reflux monitoring. Pooled clinical success rate 73%.
- Traditional delayed release PPIs should be administered 30-60 min before meal for maximal pH control
- PPI therapy should be initiated at once day dosing
- Negligible differences in efficacy between PPIs in healing erosive esophagitis or symptom relief
- Maintenance PPI therapy at the lowest effective dose for GERD patients with persistent/recurrent symptoms and in patients with complications including ERD or Barrett's esophagus
- Few response to PPIs for regurgitation, cough and laryngeal symptoms (26 to 44%)
- Adverse events for long term use PPIs. Micronutrient malabsorption, pulmonary infections, osteoporosis, bone fractures, heart disease, kidney disease and dementia. No well designed studies.

# GERD: short and long term healing rates

## Healing rates according to LA grading of esophagitis



## Remission after 6 months



# Therapy

- H<sub>2</sub>RAs is an option for GERD without erosive disease. Bedtime H<sub>2</sub>RAs can be added to daytime PPI for objective persistent night-time symptom.  
CAVE tachyphylaxis
- Baclofen reduces transient LES relaxations and reflux events. Associated with central side effects. Option in case of persistent symptoms with PPIs.
- Prokinetic therapy should not be used in GERD patients without diagnostic evaluation. No increase healing rate of ERD or symptoms. Increase risk of adverse events.
- No role for Sucralfate in the non-pregnant GERD patient. Interest in case of bile stagnation in the stomach.
- Interest of acid ursodeoxycholic in case of bile stagnation after surgery ex laparoscopic bypass

Mainie I, J Clin Gastroenterol 2008

Van Herwaarden, Aliment Pharmacol Ther 2002

Ren LH, World J Gastroenterol 2014

# PPI failure

- Maybe the wrong diagnosis...
- Lack of compliance. Overall discontinuation rate of 20% for patients with BE and 31.9% for non-BE GERD patients.
- Increase the dosage to twice per day. NNT 25.
- Optimizing PPI therapy – split or spread doses, timing of PPI therapy.
- Change in PPI therapy may help in GERD. Gastric acid suppression can differ among PPIs.
- Adding an alternate anti-reflux medication. No proven benefits

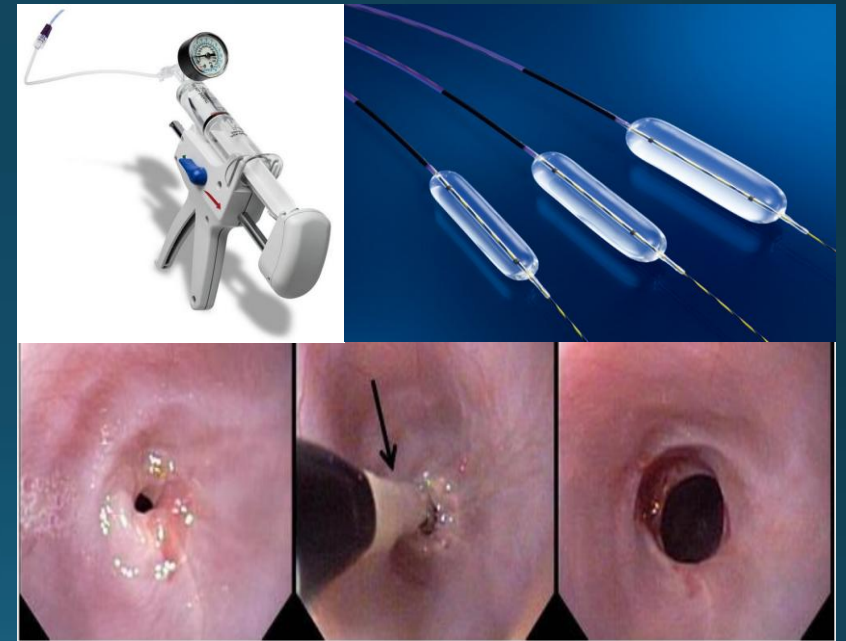
Khan M, Cochrane Database Syst Rev 2007  
El Serag HB. Am J Gastroenterol 2009  
Fass R, Clin Gastroenterol Hepatol 2006 and 2012



# Endoscopic procedures for peptic strictures

## Mechanical (push-type or bougie) and balloon dilation

- Immediate success rate for dysphagia 80% to 90%
- Recurrence rate up to 30% to 40% during long-term follow-up
- No related complications with concomitant biopsies
- Cons for bougie dilation: tight, tortuous or long stricture, large hiatus hernia, esophageal diverticulum or tracheoesophageal fistula. More risk of perforation
- 1<sup>st</sup> dilation: approximately the diameter of the stricture with a moderate or significant amount of resistance.
- 'Rule of three', performing up to three dilations that meet resistance per session, with an increase in the stricture diameter by 2 mm (6 Fr).
- Interval of session: 1 to 2 weeks
- Target lumen diameter > 18 mm
- Failure of treatment: no improvement after 6 well-conducted sessions



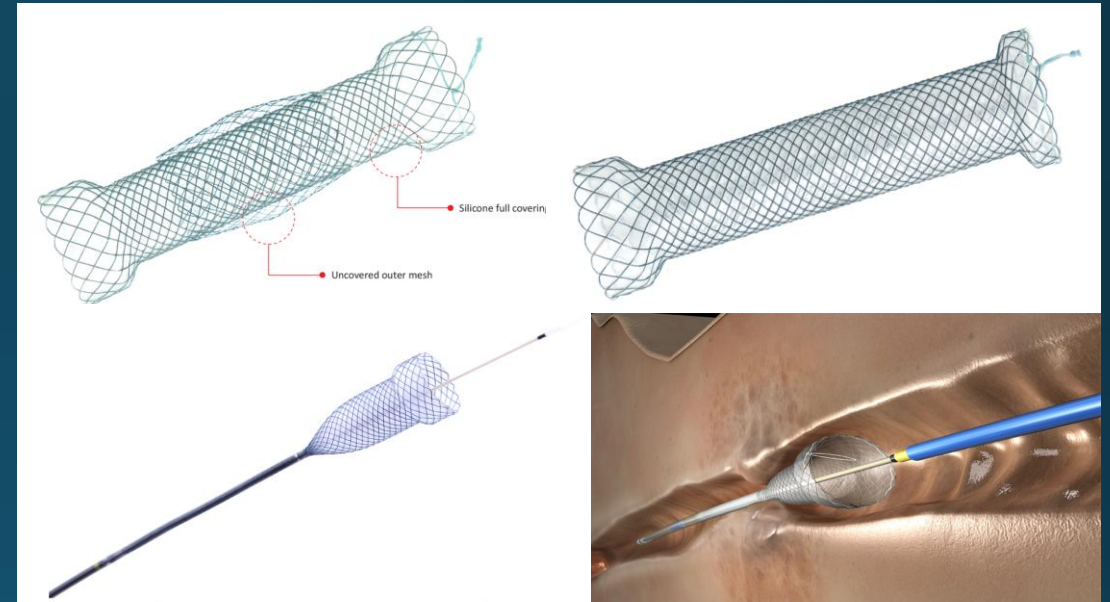
# Endoscopic procedures for peptic strictures

## Fully covered self-expanding metallic stent (SEMS)

- Technical success rate of 98% and long term clinical success rate of 45 to 50%
- Rapid relief of dysphagia
- New stents design
- Early stent migration (30%)
- Less food impaction

## Biodegradable stent

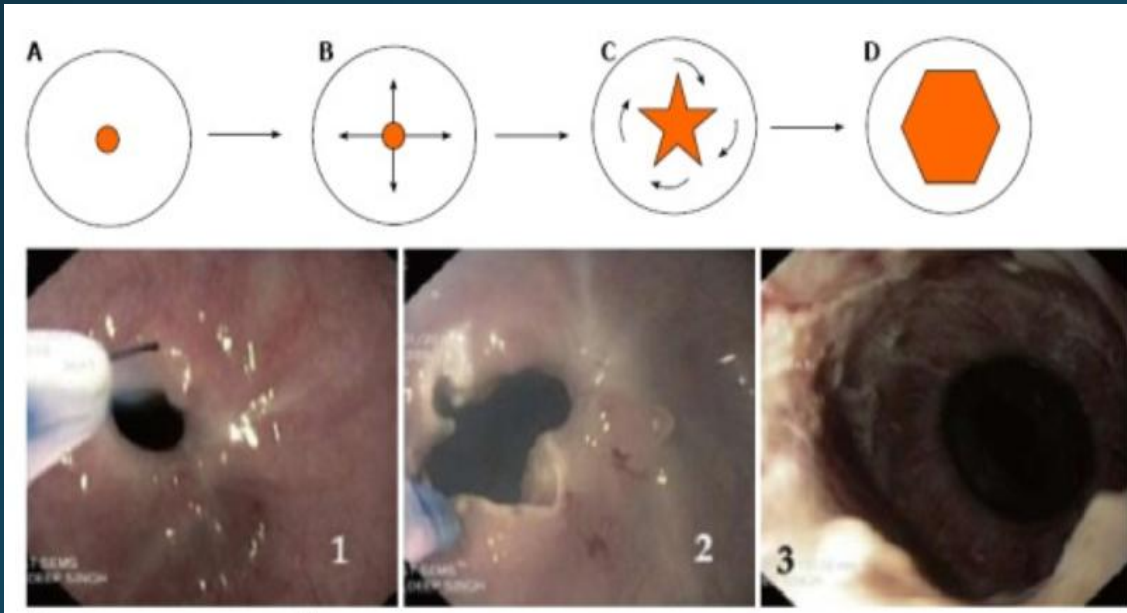
- Technical success rate of 96% and long term clinical success rate of 47%
- Tissue overgrowth/Hyperplastic reaction (20%)
- Stent impaction and food impaction
- Less early stent migration (15%)
- Painful
- No need of stent removal



Selection of stent should be individualized, taking into consideration the endoscopist's experience as well as patient and stricture characteristic

# Endoscopic procedures for peptic strictures

## Endoscopic incisional therapy



## Outcome

- Pooled clinical success rate 83%
- Perforation rate 0 to 3.5%
- Severe bleeding 0.1 to 0.4%
- Best for stricture < 1cm length
- Useful for naive or refractory stricture
- Significant increase in the mean duration of improvement immediately after one incision compared to balloon dilatation (17 mo vs 5 mo;  $P = 0.034$ )

# Surgery for GERD

- Treatment option for long term therapy in GERD patients
- Works best in typical GERD
- Preoperative manometry for all patients to rule out achalasia or scleroderma-like esophagus
- Generally not recommended for patients who do not respond to PPI therapy
- As effective as medical therapy for carefully selected patients. Lotus trial: 5 year remission rate at 92% with PPI, 85% with fundoplication (p=0.048)
- Laparoscopic Roux-en-Y gastric bypass should be considered for obese patients (BMI  $\geq 40$  or BMI  $\geq 35$  with at least 2 at least 2 obesity-related co-morbidities)
- Partial fundoplication may offer reduced dysphagia and need for reoperation (Gas bloat syndrom) with similar clinical outcomes. No long-term comparative assessment of the two approaches
- **Do not prevent progression of Barrett's to cancer.** Need an endoscopic follow-up even after fundoplicature

Galliche JP, JAMA 2011

Kethman W, J Gastrointest Surg 2017

# Laparoscopic fundoplication ± hiatal hernia repair

## Indications

Effectiveness of PPI **BUT**... patient unwilling or unable to take PPI

Persistence of disease on therapy

- Erosive esophagitis
- Persistent symptoms with + IPH study

Massive regurgitation ("volume reflux")

Large hiatal hernia



Low operation risk



Experienced surgeon

**Table 2** Most common procedure-related risks and complications associated with surgical management of reflux disease

### Procedure-related risks or complications

Pneumothorax	0–4%
Gastric or esophageal injury	0–4%
Conversion to open	0–24%
Wound infection	0.2–3.1%
Wrap migration or herniation	0.8–26%
Reoperation rates	0 to 15%
Dysphagia	5%
Recurrent heart burn	1–10%
Recurrent regurgitation	1%

Complete clinical success for heartburn and regurgitation in 75 to 80%. 43 to 62% patients still using IPP after fundoplication.



**TABLE 1.** Antireflux Procedures as Potential Alternatives to Fundoplication

Radiofrequency treatment

Stretta (Mederi Therapeutics Inc., Norwalk, CT)

Endoscopic plication or suturing

EndoCinch (C.R. Bard Inc., Murray Hill, NJ) endoluminal gastroplication (discontinued)

Plicator System (Ethicon Endo-Surgery) for endoscopic full-thickness plication

EsophyX (EndoGastric Solutions, San Mateo, CA)

Syntheon ARD plicator (Syntheon LLC, Miami, FL)

MUSE (Medigus, Omer, Israel) transoral incisionless fundoplication

Injection or implantation of bulking agents

Enteryx (Boston Scientific, Natick, MA) injectable biopolymer (withdrawn from market 2005)

Gatekeeper (Medtronic Inc., Minneapolis, MN) injectable hydrogel prosthesis (withdrawn from market 2005)

Plexiglas polymethylmethacrylate microbeads (Arkema Inc., Bristol, PA; not FDA approved)

Durasphere (Carbon Medical Technologies, St Paul, MN) injectable carbon-coated beads (not FDA approved for GERD)

Surgical alternatives

Angelchik (American Heyer-Schulte, Goleta, CA) antireflux silicone prosthesis

Linx (Torax Medical, Shoreview, MN) implantable ring of titanium magnetic core beads for sphincter augmentation placed laparoscopically around distal esophagus

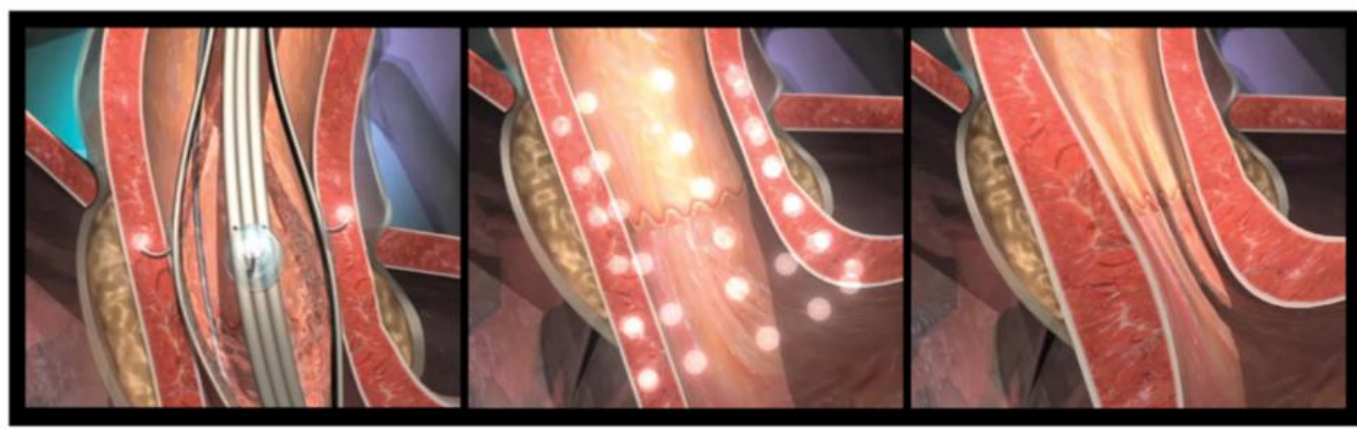
EndoStim (EndoStim, St Louis, MO) implantable bipolar electrical stimulator of LES and programmable pulse generator

FDA indicates Food and Drug Administration; LES, lower esophageal sphincter.

# Endoscopic and surgical alternatives for GERD treatment

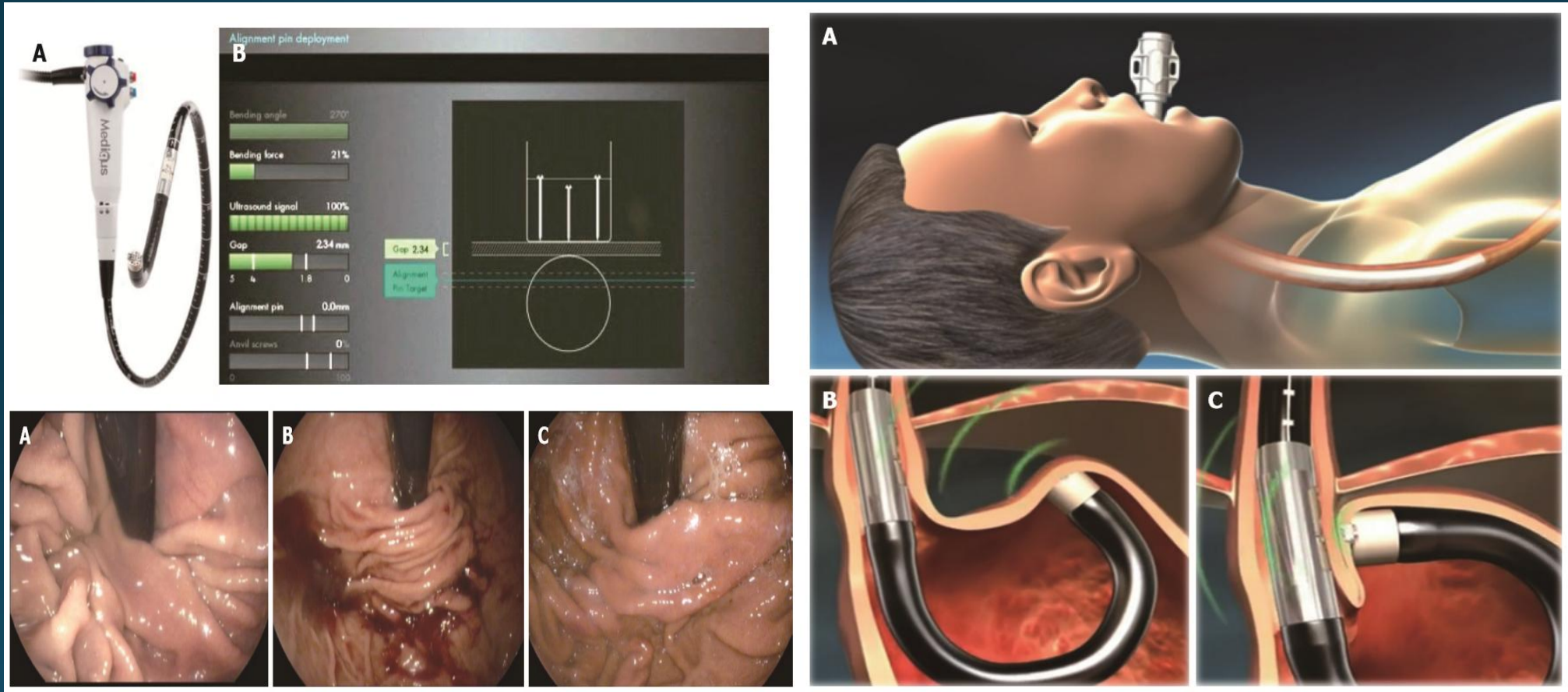


# Radiofrequency treatment. Stretta®



- 15 years experience
- Expectation of increase LES pressure and reduce TLESRs after hypertrophy and scarring of LES
- No effect on acid exposure, discontinuation of PPIs or improved in quality of life with randomized trials

# Transoral incisionless fundoplication. Muse®



# Transoral incisionless fundoplication. Muse®

## Postoperative cares

- Antiemetic prophylaxis with at least two drugs maintained intravenously for 24h
  - Broad-spectrum antibiotic therapy intravenously for 48 h, then orally for 5 days
  - Liquid diet for the first 2 weeks and a soft diet for the next 4 weeks
  - Refrain from vigorous exercise for 4 weeks
  - PPIs discontinued 7 days after the procedure
- Minor adverse events rate 5.5 to 22%
  - Major adverse events rate in 6%. Pneumothorax, esophageal leak, pneumomediastinum, bleeding
  - PPI use was stopped or halved in 77% (54% stopped PPI completely)
  - 70% normalization or  $\geq 50\%$  decrease in distal acid exposure

**Table 2 Symptomatic responses after transoral incisionless fundoplication by the MUSE™ system**

Ref.	6 mo	12 mo	24 mo	36 mo	6 yr
Zacheri <i>et al</i> <sup>[28]</sup> , 2015	83%	-	-	-	-
Roy-Shapira <i>et al</i> <sup>[29]</sup> , 2015	-	82%	73%	73%	-

# Transoral incisionless fundoplication. Muse®

## Factors affecting TIF outcomes

### Good predictive factors

- Number of stapling deployed and the rotational technique (60°-180° as long as the right-most stapling) increased by half the probability of being a responder
- ≥50 years old
- Good or partially response to IPP

### Bad predictive factors

- Pre-operative Hill grades III and IV hiatal hernia
- Hiatal hernia > 2 cm
- Ineffective esophageal motility

### Mainly realized on patients with

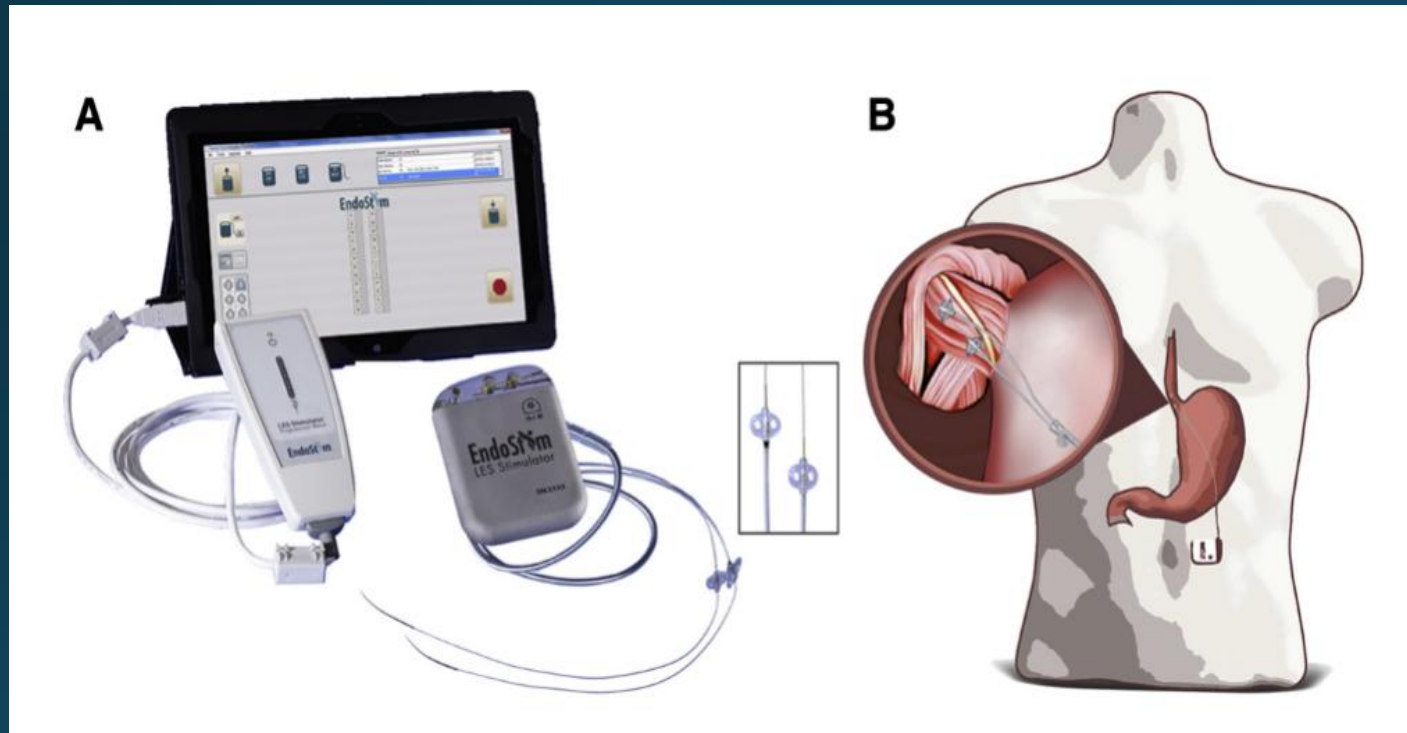
- Good or partially response to PPI
- Refuse of long term medication
- Intolerant or need of high doses of IPP
- Hiatal hernia ≤3cm
- Esophagitis LA grade B or lower
- Without Barrett's esophagus

# Magnetic sphincter augmentation. Linx®

- Laparoscopically implantation of a bracelet of titanium magnets at the EGJ
- Sized to fit varying EGJ circumference
- Indicated in well documented GERD, without hiatal hernia of  $\geq 3$ cm, esophageal dysmotility. Alternative to traditional laparoscopic fundoplication.
- Long term outcome available for up to 5 years
- Reduce acid exposure in 58% and reduction of PPIs in 85%.
- Regurgitation rate decreased from 57% to 1 % after 5 years.
- Dysphagia in 68% after 1 year and 4% after 5 years.
- Removal rate of the device of 7% due to dysphagia and chest pain.
- Device erosion rate in 1%. No knowledge about the long term consequences of having an implanted titanium bracelet.



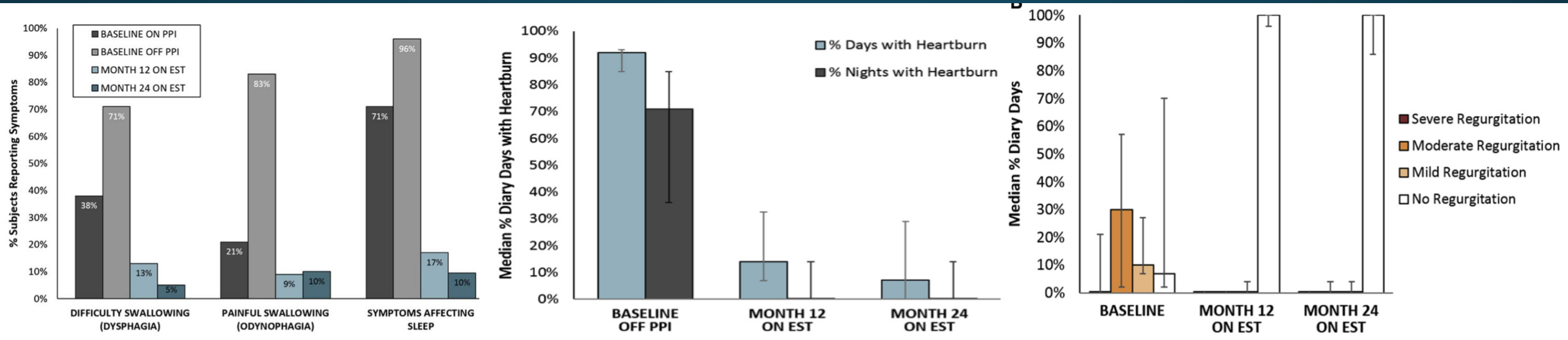
# Electrical stimulator of LES. EndoStim®



- Implanted Laparoscopically
- LES –EST 20Hz, 215  $\mu$ s, 3-8mAmp over 30 min, 6-12 sessions per day starting the day 1 after implantation
- Stimulation intensity adapted over time



# Electrical stimulator of LES. EndoStim®

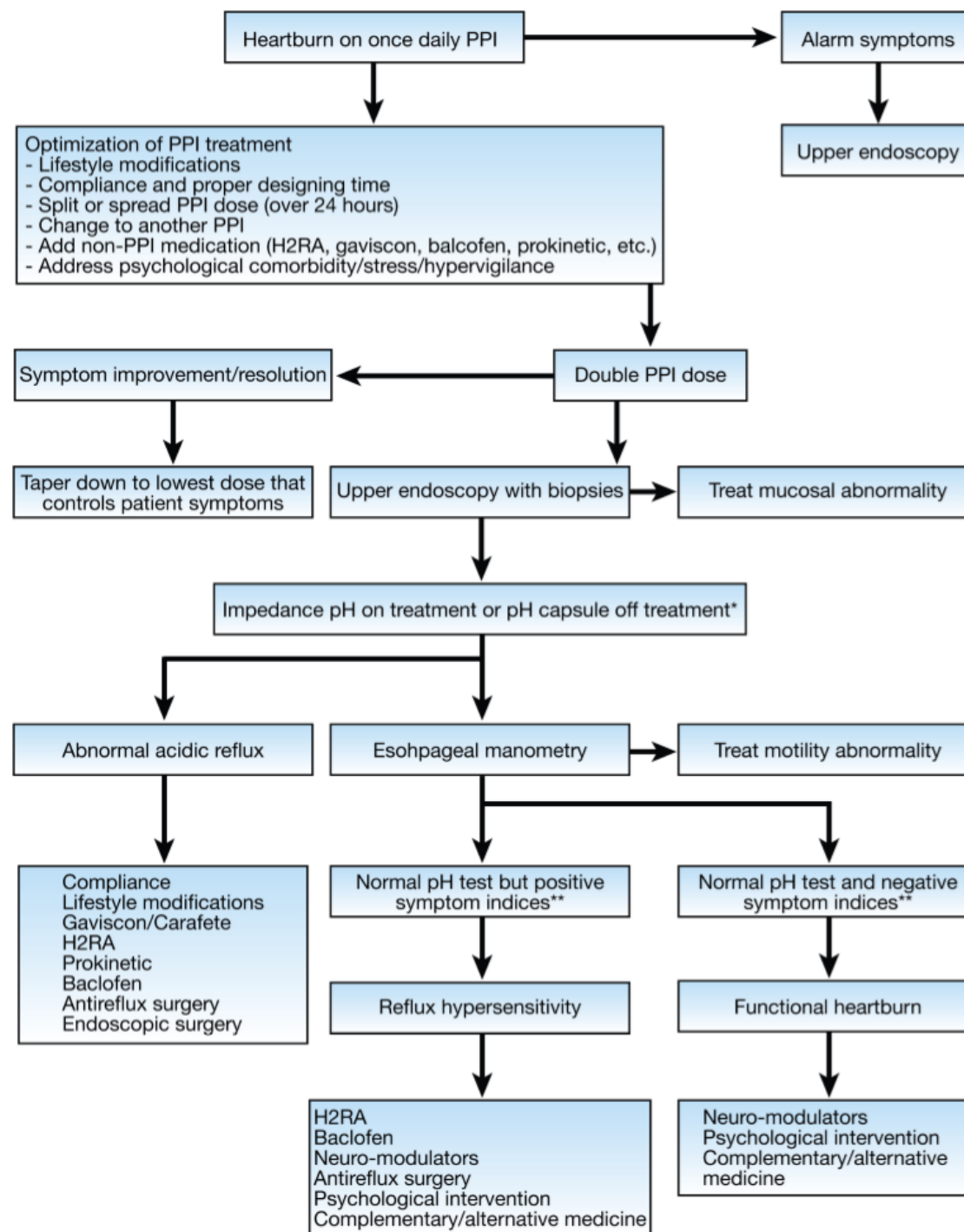


Mainly realized on patients with

- Partially response to PPI
- 24hours esophageal pH<4 for >5% of time
- Hiatal hernia ≤3cm
- Esophagitis LA grade C or lower

2 years experience

- 71% normalization or ≥50% decrease in distal acid exposure
- 76% complete cessation of PPI
- No device or therapy related serious adverse events
- Useful in case of esophagus dysmotility
- Expansive



**Thank you for your attention**